REMARKS

Applicants respectfully request entry of amendments to claims 1, 98-102, 104, 107, and 114. Please cancel claims 2-82, without prejudice or disclaimer. Support for the amendments can be found throughout the specification, including paragraphs [0013], [0015], [0016], [0023], and the originally filed claims and, therefore, do not add new matter.

Applicants have also provided herewith, a Declaration under 37 C.F.R. §1.132 from the co-inventor, Dr. Tony N. Frudakis, to support arguments in response to the obviousness rejections of record.

Applicants submit that pending claims 1 and 83-115 are in condition for allowance, and respectfully request that the claims as amended be entered.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1 and 83-115 stands rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Claim 1 is alleged to be indefinite for lacking antecedent basis for the recitation "SNPs hybridizing in step (b)." While not acquiescing to the reasoning offered in the Action, in order to expedite prosecution toward allowance, the claim has been amended such that the antecedent basis for the term is clear.

Claim 1 is also alleged to be indefinite for the recitation "a SNP which may be correlated with but not linked to a gene-linked trait." Applicants submit that this allegation is incorrect.

In Exxon Research & Engineering Co. v. United States, 60 U.S.P.Q.2d 1272 (Fed. Cir. 2001) the court stated that "the standard for assessing whether a patent claim is sufficiently definite to satisfy the statutory requirement as follows: If one skilled in the art would understand the bounds of the claim when read in light of the specification, then the claim satisfies section 112 paragraph 2." Review of the instant specification for the term in question recites the following:

"Previously, efforts have been made to control the two sources of population structure, including sampling effects and natural human demography, which were believed to confound efforts to identify markers of genes associated with particular traits. However, as disclosed herein, population structure is reflective of human demography, and markers that correlate with a trait value are useful as reporters of structure that correlate with trait value (rather than markers in LD with phenotypically active loci), and, therefore, provide a valuable tool that enables accurate classification in a cost-effective and practical manner." (Paragraph [0069]).

Thus, one of skill in the art would understand that for population structure analysis, SNPs can be associated with a numerical quality assigned to a distinguishing characteristic (i.e., trait value; e.g., human demography) as opposed to an active gene which associates with linkage disequilibrium (e.g., gene variants which correlate with disease). As such, one of skill in the art would understand the metes and bounds of the claim element in view of the specification. Accordingly, "the claim satisfies section 112 paragraph 2."

Claim 1, step (f) is alleged to be indefinite, as the metes and bounds of the term "proportional ancestry" are purported to be unclear. Applicants respectfully submit that the allegation is incorrect.

The specification clearly defines the term "proportional ancestry" as follows: "As used herein, the term "proportional ancestry" refers to the percent contribution of each (if more than one) ancestral group to which an individual belongs." (Paragraph [0167]). As the specification explicitly provides a definition for the term, one of skill in the art would understand the metes and bounds of the term, and thus, the claim is not indefinite.

Claim 84 is alleged to be indefinite, as the metes and bound of the term "determining an Fst >0.4" is unclear. "Fst" is an art recognized term which means Fixation index (F_{ST}), which is a measure of population differentiation based on genetic polymorphism data (such as SNPs or microsatellites).[1] As such, one of skill in the art would understand how to determine such a

[1] See, e.g., <http://en.wikipedia.org/wiki/Fixation_index>, last visited, December 12, 2007.

value, and thus, one of skill in the art would understand the metes and bounds of the term, therefore, the claim is not indefinite.

Claim 91 is alleged to be indefinite, as the metes and bounds of the recitation "maximizes a cumulative delta value between, and minimizes a difference in cumulative delta value within, each of the one or more pairs of the population." Again, as stated in Exxon, "the standard for assessing whether a patent claim is sufficiently definite to satisfy the statutory requirement as follows: If one skilled in the art would understand the bounds of the claim when read in light of the specification, then the claim satisfies section 112 paragraph 2." Review of the instant specification for the term in question recites the following:

> "The collection of 71 AIMs used for in this Example was selected to maximize the cumulative δ value within, and minimize differences in the cumulative δ value between each of the six possible pairs of the four dimensional (sub-Saharan African, Native American, IndoEuropean and East Asian) problem. The algorithm inverts the population specific allele frequencies to obtain a likelihood estimate of proportional affiliation corresponding to a multilocus genotype using three groups at a time (mainly for computational convenience and because a 4-dimensional admixture is likely to be relatively rare). For example, the likelihood of 100% IndoEuropean, 0% Native American, 0% East Asian is calculated, then the likelihood of 99% IndoEuropean, 1% Native American, 0% East Asian is calculated next, and so on until all possible IndoEuropean, Native American and East Asian proportions are considered, then the process is repeated for all possible IndoEuropean, Native American and African proportions, and all possible Native American, African and East Asian proportions. The likelihood of maximum value is selected as the Maximum Likelihood Estimate (MLE)." (Paragraph [0232]).

Thus, one of skill in the art would understand that for population structure analysis, this process, as claimed, achieves likelihood estimates to obtain a Maximum Likelihood Estimate, and can be performed by an algorithm as disclosed. As such, one of skill in the art would

understand the metes and bounds of the claim element in view of the specification. Accordingly, "the claim satisfies section 112 paragraph 2."

Claim 1 is also allegedly indefinite for omission of essential elements listed as (1) a step directed to "determining the nucleotide occurrences of a first population of SNPs" and (2) determining minor allele frequencies of SNPs, between step (b) and step (c). Regarding the first item, while Applicants do not acquiesce to the reasoning offered in the Action, in order to expedite prosecution toward allowance, the claim has been amended to substantially recite the first item. However, regarding the second item, Applicants respectfully submit that the Action is incorrect.

For indefiniteness analysis, alleged unclaimed essential matter is determined by demonstrating that a claim fails to interrelate essential elements of the invention as defined by Applicants in the specification. (M.P.E.P. §2172.01).

Applicants respectfully submit that the specification is not written for the layperson, but for those skilled in the art (see, e.g., Ajinomoto Co., Inc. v. Archer-Daniels-Midland Co., 56 U.S.P.Q. 2d 1332 (Fed. Cir. 2000)). Accordingly, because delta value measures the difference in minor allele frequency between various populations, one of skill in the bioinformatics art, to which this invention belongs, would appreciate that the minor allele frequencies would have been determined to generate the delta values (see, e.g., paragraph [0189]), therefore, there is no "gap" between steps (b) and (c). Since there is no demonstration provided by the Action which shows that Applicants have failed to interrelate essential elements of the invention as defined in the instant specification, there is no *prima facie* case for indefiniteness.

For these reasons, Applicants respectfully request that the rejections be withdrawn.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1 and 83-115 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking written description support.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

The Office Action alleges, in pertinent part, that the specification does not disclose "non-parental." While not acquiescing to the reasoning offered in the Action, in order to expedite prosecution toward allowance, the claims have been amended to recite "test" individual. The term can be found throughout the specification as filed, including paragraphs [0013], [0015]-[0019], [0023], and the original claims.

For these reasons, Applicants respectfully request that the rejection be withdrawn.

Rejections Under 35 U.S.C. §103

Claims 1, 84-86, 90, 92-97, 100, 104, and 105 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Parra et al. in view of Ott et al. and Halushka et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Parra et al. is silent with respect to teaching the selection of a second group of SNPs with minor allele frequencies > 1% and that they do not specifically disclose the BGA comprising East Asian ancestral groups. The Action then provides Ott et al. and Halushka et al. to cure the deficiency identified in the primary reference, reciting that the former teach selection of a subset and the latter teach a method for selecting SNPs informative of hypertension with minor allele frequencies > 1%, including that Halushka et al. teach coding and non-coding regions. However, review of the combination demonstrates that the references do not teach neutral markers: i.e., those that correlate with trait value rather than markers in linkage disequilibrium (LD) with phenotypically active loci, an element presently recited in the claims.

Applicants respectfully submit that the position that Halushka et al. teach "non-coding regions" as an example of neutral markers shows a misapprehension of the allegedly identical element as claimed (i.e., at least one of the second population of SNPs is a SNP which may be correlated with but not linked to a gene-linked trait, and wherein the at least one SNP of the second population of SNPs is not located within a gene encoding region). 5'UTRs, introns and

3' UTRs are parts of an active gene; i.e., they are associated with markers in LD with phenotypically active loci.

As stated in the present specification at paragraph 6:

> "Investigators generally have been concerned with identifying gene variants that cause a disease (the so called "phenotypically active" loci), rather than identifying gene variants that are simply correlated with disease. As such, whatever the trait being examined, and for most study designs involving unrelated individuals, it has been considered important to control for population structure so as to avoid identifying markers of structure that correlate with trait value in a given sample rather than those in linkage disequilibrium (LD) with phenotypically active loci (Risch et al., *Genome Biology* 3:1-12, 2001 Wang et al., *Amer. J. Hum. Genet.* 71:1227-1234, 2002; Burroughs et al., *supra*, 2002; Rao and Chakraborty, *Amer. J. Hum. Genet.* 26:444-453, 1974). There are two sources of population structure in a sample collection: 1) sampling effects, which can create structure even if sampling is performed from homogeneous populations, and 2) natural human demography. The first source of population structure is a nuisance for genetics studies, and associations found from a study due to this type of structure are generally considered an artifact of the collection process rather than a reflection of human demography. Most geneticists generally consider the second kind of structure to be a nuisance as well. As such, associations identified as being due to population structure have been considered spurious findings or artifacts, and have generally been discarded; only findings due to true linkage or LD have been published, as such markers are considered linked to biologically relevant genes."

Accordingly, the prior art did not recognize the usefulness of a SNP which may be correlated with but not linked to a gene-linked trait; i.e., all measures of population-to-population genetic contribution relied on genetic markers that were found in gene sequences, since most of the research prior to the completion of the human genome draft was based on the hypothesis that gene sequences cause disease. Applicants submit that gene sequences which are associated with

markers in LD with phenotypically active loci cannot be used to measure ancestry because they are acted upon specifically by evolution. Measuring such gene sequences may assist in the study of the evolution of phenotypes relevant to those genes, or the convergent evolution of populations, but cannot provide interpretable information about ancestry.

As stated in Bamshad et al. (Deconstructing the Relationship between Genetics and Race, Nature Rev Genetics (2004) 5:598-609), "[i]nferences of human population structure based on genetic data often differ from inferences based on phenotypic characteristics." (Id., at 601). They go on to say that:

> "For instance, although facial features and skin pigmentation [i.e., phenotypic traits] are routinely used to group people by race, populations that share similar physical characteristics as a result of natural selection can differ genetically. For example, the degree of skin pigmentation in some sub-Saharan African, South Indian and Melanesian populations is similar because of adaptive evolution. But, genetically these populations are quite dissimilar. By contrast, the Ainu of northern Japan are morphologically different (for example, they have less skin pigmentation and more body hair) from other East Asian populations, but are genetically very similar to them. Overall, the degree of differentiation in quantitative traits often exceeds that observed for neutral markers, indicating that quantitative traits have been subject to natural selection. Therefore, their distribution does not necessarily reflect the distribution of neutral markers nor are they good predictors of group membership. Indeed these characteristics might imply that there is a closer degree of relatedness than exits or vice versa." (Id.) (Emphasis added).

As can be seen from the above, resolving the ancestry from the environment is not possible using only gene-linked sequences. As an extreme example, if markers within pigmentation genes are used, measures of "ancestry" could (depending on the markers selected) reveal South Asians and African populations as seemingly sharing relatively recent common

ancestry to the exclusion of other lighter-skinned Eurasian populations. It is clear from the paleoarchaelogical and linguistics record that this would be an incorrect "answer." Ironically, Parra et al. used a number of markers in pigment genes - the GC gene is involved in Vitamin D homeostasis which is relevant to human pigmentation (Jobling et al., Human Evolutionary Genetics Origins, Peoples and Disease, 2004, Garland Publishing, New York, NY) and OCA2 is a human pigmentation gene primarily responsible for human iris color (Frudakis et al., Genetics. (2003)165(4):2071-83; Frudakis et al., Hum Genet (2007) 122(3-4):311-26; Frudakis Molecular Photofitting: Predicting ancestry and phenotype using DNA, 2007, Elsiever/Academic Press Publishers, Burlington, MA), as well as skin color. As these markers are all gene-linked (i.e., quantitative markers), these measures are therefore not good predictors of ancestry (see Bamshad et al., *supra*).

For example, the markers used in Parra et al. (i.e., APO A; apolipoprotein A; AT3, antithrombin 3; FY [DUFFY antigen]; D115429, intron sequence; OCA2, tyrosinase mutation; RB1 retinoblastoma gene (non-suppression); micro RNA; and GC, vitamin D binding protein) are all, without exception, gene-linked. Again, the method as claimed requires that at least one SNP correlate with trait value rather than markers in linkage disequilibrium (LD) with phenotypically active loci. This deficiency is not cured by either of the secondary references.

Ott et al., for example, also focuses on genetic variations found within genes and selection from among them for enhancing the power of disease-gene research, but do not teach how ancestry can be properly assessed. The paper acknowledges that false positive associations may result from population structure (see, e.g., p. 285, col. 1, "**INTRODUCTION**"), but does not teach how this structure can be ameliorated, how ancestry can be measured apart from phenotype, or how true ancestral informative markers (AIMs) can be identified. The statistical tests described in Ott et al. are as adept at identifying false positives caused by (unobserved) population structure as they are at identifying markers associated with phenotypes, yet do not distinguish between the two.

Hulushka et al. uses self-assessed "race" or "ethnicity" as a means by which to select SNPs located within genes. Since all of the SNPs described in this study are located within genes (as stated above, 5'-, 3'- UTRs and introns are parts of genes), ancestry is not assessed and

the selection of AIMs not described. Indeed, as the reference states that "overall, the degree of nucleotide polymorphism across these genes, and orthologous great ape sequences, is highly variable and is correlated with the effects of functional conservation on gene sequences" (see, e.g., p. 239, Abstract), this indicates that their results speak specifically to the evolution of phenotype rather than in the assessment of (true) ancestry. Accordingly, neither of these references cures the deficiencies identified above for Parra et al.

Applicants submit that, in fact, the cited references "teach away" from the present invention. One of skill in the art would only extract from such teachings confounded relationships due the exclusive use of markers strictly coupled to phenotype or geography . As such, the references do not teach the purpose of determining ancestry by using SNPs that are not linked to a gene-linked trait, and thus, the purpose of Applicants' invention could not be accomplished using the teachings of the cited references. Therefore, the references teach away, since the impression left to the skilled artisan is that the method would not have the property sought by Applicants. In re Caldwell, 319 F.2d 254, 256, 138 USPQ 243, 245 (CCPA 1963).

Applicants submit, not merely as a theoretical proposition, that because the use of SNPs that are not linked to a gene-linked trait is ultimately required *as a requisite property* of the present method, in view of the teachings of Parra et al., Ott et al., and Halushka et al., determination of true ancestry becomes an impossibility.

Further, as there is no suggestion or expectation of success regarding the use of SNPs that are not linked to a gene-linked trait, whether Parra et al. teach or do not teach fitting genotype frequencies to Hardy-Weinberg proportions or suggest or do not suggest the selection of genetic markers that show homogeneity with Africa and Europe, to allege the obviousness of minor allele frequency calculations, is immaterial.

It is axiomatic that one cannot simply use the Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). As there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Since the teachings of Parra et al. would not result in a method for determining ancestry as claimed when combined with the teachings of Ott et al. and Halushka et al., one of skill in the art would not have an expectation of success because the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claims 87-89 and 110-115 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Parra et al., in view of Ott et al. and Halushka et al., and in further view of Sorenson et al.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The deficiencies identified in the combination of Parra et al., in view of Ott et al. and Halushka et al. have been covered above, and will not be reiterated here.

The Office Action alleges, in pertinent part, that the combination of Parra et al. in view of Ott et al. and Halushka et al. is silent with respect to teaching the number of SNPs as recited in claims 87-89, or a photo of a person from whom the known proportional ancestry was determined as in claims 110-115. The Action the provides Sorenson et al., which is alleged to teach a genealogical research and record keeping system for identifying commonalities in haplotypes from biological samples that correlate with markers and a trait. As the Sorenson et al. reference was not filed before the priority date claimed for the present application, the reference is not available as prior art, thus, no prima *facie case* of obviousness can been established in view of the Sorenson et al. reference.

Again, because the teachings of Parra et al. would not result in a method for determining ancestry as claimed when combined with the teachings of Ott et al. and Halushka et al., one of skill in the art would not have an expectation of success because the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claims 97-99, 101-103, and 106-109 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Parra et al., in view of Ott et al. and Halushka et al., and in further view of Kanetsky et al., Pritchard et al. (A) and Pritchard et al. (B).

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The deficiencies identified in the combination of Parra et al. in view of Ott et al. and Halushka et al. have been covered above, and will not be reiterated here.

The Office Action alleges, in pertinent part, that the combination of Parra et al. in view of Ott et al. and Halushka et al. is silent with respect to teaching BGA for an Asian ancestral group, as in claims 98-99, and 107-109, four group comparisons, as in claim 101, or the graphical representation as in claims 102 and 103, or generating an ancestral map, as in claim 106. The Action the provides Kanetsky et al., which is alleged to teach SNP markers for coding and non-coding regions in white, African, Spanish, Hispanic, Native American, Aboriginal, and Asian populations for investigating relationships of hair and eye color, as in claims 98, 99, 101, and 107-109. As the Kanetsky et al. reference was not available before the priority date claimed for the present application, the reference is not available as prior art, thus, no prima *facie case* of obviousness can been established in view of the Kanetsky et al. reference.

Nevertheless, Kanetsky et al. use SNP markers within gene regions, many of them human pigmentation genes. Further, while claiming to "investigate ancestral relationships of hair and eye color," they are in fact investigating the history of phenotypes, rather than the history of humans and human populations. Graduating from the former to the latter is not obvious for reasons already explained. Indeed, since phenotypes were not properly assessed, Applicants submit that the teaching of Kanetsky et al. represent non-analogous art with respect to teaching ancestry as claimed.

As the Pritchard et al. (A) reference was not available before the priority date claimed for the present application, the reference is not available as prior art, thus, no prima *facie case* of obviousness can been established in view of the Pritchard et al. reference. Nevertheless, the Action then offers Pritchard et al. (A), which is alleged to teach methods for inferring population structure and calculation of likelihood test statistics, means for graphically displaying ancestral results in triangular format, and a computer-based program STRUCTURE to estimate population structure. Moreover, the Action offers Pritchard et al. (B), which is alleged to show statistical methods for determining ancestral maps and correspondence to proportional ancestry. However, neither Pritchard et al. (A) nor Pritchard et al. (B) teach the use of SNPs that are not linked to a gene-linked trait, therefore whether Pritchard et al. (A) or (B) teach or do not teach the statistical methods as disclosed in the Action is immaterial. Accordingly, Applicants respectfully submit that neither Kanetsky et al., Pritchard et al. (A) nor Pritchard et al. (B) cure the deficiencies identified above for the combination of Parra et al., Ott et al. and Halushka et al.

Again, because the teachings of Parra et al. would not result in a method for determining ancestry as claimed when combined with the teachings of Ott et al. and Halushka et al., which is not cured by Kanetsky et al., Pritchard et al. (A) or Pritchard et al. (B), alone or in combination, one of skill in the art would not have an expectation of success since the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus,

no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Claims 1, 83-91, 95-99, and 107-110 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Shriver et al. in view of Daly et al. and Kruglyak.

Applicants traverse the rejection as it might apply to the amended claims, including claims dependent therefrom, for the reasons given below.

Applicants submit that because the cited references do not teach all the claim limitations, one of skill in the art would not be motivated to combine the reference teachings.

The Office Action alleges, in pertinent part, that Shriver et al. is silent with respect to teaching the use of SNP markers or the selection of a second group of SNPs with minor allele frequencies > 1%, as in claims 1, 87-89 and 107-110. The Action then provides Kruglyak, which allegedly teaches the use of SNPs as biallelic markers over microsatellite markers to provide rapid automated genotyping for linkage studies, as well as assays with high-density microarrays. Further, Daly is provided, which allegedly teaches a method for selecting a subset of 103 rare SNP markers with minor allele frequencies of >5% from a Canadian population to provide an improved resolution picture of genetic variation and transmission of Crohn's disease linkage disequilibrium analysis. However, review of the combination demonstrates that the references do not teach neutral markers: i.e., those that correlate with trait value rather than markers in linkage disequilibrium (LD) with phenotypically active loci, an element presently recited in the claims.

Shriver et al. used markers from genes. The fact that many of these genes were human pigmentation genes reinforces their lack of utility for genomic ancestry, as described above. As such, Shriver et al. disclose methods useful for the study of the evolution of gene sequences and phenotypes rather than ancestry. As neither Daly et al. nor Kruglyak cure the deficiencies identified in Shriver et al., whether Daly et al. teach or do not teach a method for selecting a subset of 103 rare SNP markers with minor allele frequencies of >5% from a Canadian population to provide an improved resolution picture of genetic variation and transmission of Crohn's disease linkage disequilibrium analysis or whether Kruglyak teaches or does not teach

the use of SNPs as biallelic markers over microsatellite markers to provide rapid automated genotyping for linkage studies, is immaterial.

It is axiomatic that one cannot simply use the Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim. See, e.g., Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). As there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Since the teachings of Shiver et al. would not result in a method for determining ancestry as claimed when combined with the teachings of Daly et al. and Kruglyak, one of skill in the art would not have an expectation of success because the invention as claimed would not be achieved in view of such teachings. Therefore, one of skill in the art would not be motivated to combine such teachings.

Applicants submit that because there is no reasonable expectation of successfully achieving the invention as claimed, there is no motivation to combine the cited references, thus, no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that the rejection, including as it might be applied against the amended claims, be withdrawn.

Conclusion

Applicants submit that pending claims 1 and 83-115 are in condition for allowance. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this submission.

No fee is deemed necessary with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees required by this submission, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number.

Respectfully submitted,

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